REMARKS

Claims 1-14 are currently pending. Applicants thank the Examiner for considering the information disclosure statement.

The Office Action objected to the Abstract not being limited to a single paragraph. In response, Applicants have amended the Abstract to encompass a single paragraph and corrected typographical errors.

Claims 5 and 6 were objected to for using the undefined abbreviation "AAc" and misspelling "Phenstin". Applicants have replaced the abbreviation with the phrase "phenstatin that is acrylated to form phenstatin acrylate and then," and corrected the spelling of Phenstatin.

Claims 4, 6, and 7-12 are rejected under 35 U.S.C. 112, second paragraph. Claim 4 is cancelled. Claim 6 depends from claim 5 which introduces the term phenstatin acrylate. Therefore, claim 6 is believed to be in correct form under 35 U.S.C. 112, second paragraph.

Claim 7 also lacked an antecedent basis for the limitation phenstatin acrylate. Applicants have changed the dependency to claim 5 which is the basis for phenstatin acrylate.

Claim 9 recited the limitation "the compound," which has no antecedent basis. As proposed by the Examiner, Applicants have changed the phrase to recite a drug delivery system.

The Office Action rejects claims 1-4, 6-8, and 13-14 under 35 U.S.C. 103 as being unpatentable over the WO9934788 publication in view of Hatefi.

The Office Action states that the WO9934788 publication discloses a pharmaceutical composition containing phenstatin and

that the composition containing phenstatin may be used for inhibiting cancer cell growth.

Claim 1 recites a drug delivery system for localized delivery of phenstatin to a tumor *in vivo* comprising the polymer poly(N-isopropylacrylamide) chemically bound to phenstatin. Applicants can identify no part of the WO9934788 publication that discloses localized delivery of phenstatin to a tumor *in vivo*. While the WO9934788 publication discloses many compositions and routes of administration of phenstatin, e.g. see pages 21-29, the reference does not disclose administration directly into the tumor itself, as recited in claim 1.

Moreover, as acknowledged by the Examiner, the WO9934788 does not teach or suggest the polymer poly(N-isopropylacrylamide) chemically bonded to phenstatin, as recited in claim 1. Instead, the Examiner relies on Hatefi to allege that claim 1 is obvious under 35 U.S.C. 103.

With respect to Hatefi, the Office Action states that Hatefi discloses "that poly(NIPAAM) is a thermosensitive polymer which exhibits lower critical solution temperature at about 32 degrees Celsius … for use in *in situ* setting drug delivery." (citing page 18, 2d column, first full paragraph).

Applicants submit the Hatefi reference fails to disclose the polymer poly(N-isopropylacrylamide) chemically bonded to phenstatin. Hatefi does not specifically mention the polymer chemically bonded to phenstatin. Accordingly, Hatefi does not serve as evidence of the alleged obviousness of claiming the polymer poly(N-isopropylacrylamide) chemically bound to phenstatin.

Moreover, Applicants respectfully point out that further down the second column on page 18, Hatefi expressly warns against using such a compound for implantation purposes:

> "[A]crylamide based polymers with quaternary ammonium in their structure, in general, *are not suitable for implantation purposes due to cell toxicity* [128]. The observation that acrylamide-based polymers activate platelets on contact with blood [129], along with the poorly understood metabolism of polyNIPAAM and its non-degradability [130], make it difficult to win FDA approval. Therefore, the vast majority of the drug delivery systems which employ LCST, use block copolymers of poly(ethylene oxide)(PEO) simply because of FDA approval." (emphasis added)

In fact, the Hatefi reference would lead the person skilled in the art, viewing the prior art in July 2002, *away* from using polyNIPAAM, which would be very problematic for localized implantation, particularly in comparison with other known LCSTs.

Given the additional information cited above, a skilled person would not combine polyNIPAAM (an inferior NCST with better mentioned alternatives) with phenstatin whose administration is taught in many ways in the WO9934788 publication, but none of those ways include injection into a tumor. In addition, there is no teaching in the WO9934788 publication or Hatefi, taken singularly or in combination, that would lead one to chemically bond the polymer poly(N-isopropylacrylamide) to phenstatin.

Therefore, claim 1 is believed to patentably distinguish over the WO9934788 publication and the Hatefi reference, taken singularly or in combination. Claims 2, 3, and 5-14 are

believed to be in condition for allowance as each is dependent from an allowable base claim.

Applicant(s) believe that all information and requirements for the application have been provided to the USPTO. If there are matters that can be discussed by telephone to further the prosecution of the Application, Applicant(s) invite the Examiner to call the undersigned attorney at the Examiner's convenience.

The Commissioner is hereby authorized to charge any fees due with this Response to U.S. PTO Account No. 17-0055.

Respectfully submitted,
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